RENAL CORTICAL TRANSIT TIME AS A PREDICTOR FOR PYELOPLASTY IN PAEDIATRIC PATIENTS WITH UNILATERAL HYDRONEPHROSIS

AT THE RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL

By

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DECLARATION

I, Stuart Setjhaba More, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university. I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature: Signed by candidate

Date: 9 January 2018

ACKNOWLEDGEMENTS

Ad Majorem Dei Gloriam!

Thanks be to God for the completion of this work.

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To the Radiographers at Red Cross War Memorial Children's Hospital Department of Nuclear Medicine, Fatgiya Smith and Mark Jassen, for their assistance and support in the initial phases of this study.

To my family for their continued prayers and support during this work.

ABSTRACT

Background:

Majority of patients with unilateral hydronephrosis (HN) detected on ultrasound (US) do not require pyeloplasty. Indications for pyeloplasty are in patients with symptomatic obstruction (recurrent flank pain), complications such as urinary tract infection, a drop in differential renal function (DRF) of more than 10% and a progressive increase in the anterior posterior diameter (APD) in subsequent studies. Schlotmann et al, Piepsz et al and Harper et al have demonstrated the measurement of the cortical transit time (CTT) to predict the need for patient who may require pyeloplasty.

Objectives:

To assess if the CTT would have predicted a drop in DRF in patients with unilateral HN on the affected side. In addition to assess whether the CTT would differ on the first renogram between those patients who had a pyeloplasty and those who did not have a pyeloplasty at the Red Cross War Memorial Children's Hospital (RCWMCH).

Methods:

Sixty eight (68) patients with at least two renograms with unilateral HN with a normal contralateral kidney were observed retrospectively between December 2000 and May 2015. The CTT was recorded for the upper, middle and lower third of each kidney and the mean used as the CTT of the kidney. Each renogram was processed three times to measure the DRF using the Rutland Patlak and Integral methods. The mean of the three DRF measurements was used for analysis.

Results:

The mean CTT of the left and right hydronephrotic kidneys were 6.0minutes and 6.7minutes respectively. A significant relationship was demonstrated in the CTT and DRF as well as CTT and APD in the first renogram of those patients who did not have a pyeloplasty ($p < 0.05$). There was no difference between the DRF of the first and second renograms in those patients who did not have a pyeloplasty.

In the 20 patients who had a pyeloplasty, there was a drop of more than 10% in the DRF of 3 patients. No difference was seen in the DRF or in the CTT between the first and second renogram. The CTT was shorter in the second renogram in 9 of the 20 patients who had a pyeloplasty.

No significant difference was found in the CTT or DRF when comparing the group who had surgery against the group who did not have surgery.

Conclusion:

The current study was unable to demonstrate in our series of patients that CTT can predict those patients who would require pyeloplasty. This may be owing to the retrospective nature of the study and the reliance on the clinical notes for the US data and surgical notes. In future, a prospective study evaluating the relationship between CTT and a drop in the DRF should be undertaken in this unit.

LIST OF ABBREVIATIONS

^{99m}Tc-MAG3	Technetium 99m mercaptoacetyltriglycine
APD	anterior posterior diameter
CTT	cortical transit time
DRF	Differential Renal Function
EANM	European Association of Nuclear Medicine
HN	hydronephrosis
NaCl	Sodium Chloride
PUJ	pelvi-ureteric junction
RCWMCH	Red Cross War Memorial Children's Hospital
ROI	Region of interest
RP	Rutland Patlak
US	Ultrasound
USA	United States of America
VUR	vesicoureteral reflux

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PUBLICATION READY MANUSCRIPT
(See appendix IV for South African Journal of Surgery author guidelines)

Title: Renal Cortical Transit Time as a predictor for pyeloplasty in paediatric patients with unilateral hydronephrosis at the Red Cross War Memorial Children's Hospital

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Conflicts of interest: We have no competing interests

Main manuscript

Introduction

In 2002, Josephson critically reviewed 6 patient series chosen on the basis of a diagnosis of antenatally detected hydronephrosis, compliance with defined criteria and publication during the 1990s to allow for a longer follow-up and better diagnostic tools. He found that 88-90% of patients with unilateral hydronephrosis (HN) detected antenatally do not require a pyeloplasty[1]. In the same year, Ulman et al[2] reported that in their study population of 104 patients with antenatally detected severe unilateral HN, 22% required surgical intervention to prevent loss of renal function. The generally accepted indications for pyeloplasty are symptomatic obstruction (recurrent flank pain), complications such as urinary tract infection, a decrease in Differential Renal Function (DRF) of more than 10%, and a progressive increase in the anterior posterior diameter (APD) in subsequent ultrasound (US) studies[3]. The accepted methods for calculation of the DRF in Technetium 99m mercaptoacetyltriglycine (^{99m}Tc MAG3) renography are the Rutland-Patlak (RP) and the integral methods. In the integral method, the DRF is calculated from the background corrected area under the renogram curve between 1- 2 minutes after injection of ^{99m}Tc MAG3. The DRF calculated by the RP plot method is estimated from the mean slope of the ascending portion of the curve plotting the background corrected kidney region of interest (ROI) counts divided the cardiac ROI counts as a function of the integral of the cardiac ROI counts divided by the cardiac ROI counts[4]. The size of the APD on US is used to classify the severity of HN and is a useful predictor for the resolution of HN[5]. Accurate, repeated postnatal evaluation is therefore required to identify hydronephrotic kidneys that require surgical intervention. Recently, Schlotmann et al[6], Piepsz et al[7] and Harper et al[8] have

demonstrated that the measurement of the cortical transit time (CTT) can be used to predict the need for pyeloplasty.

The purpose of this retrospective study was to assess if the criteria used by Schlotmann et al[6], Piepsz et al[7] and Harper et al[8] would have predicted a drop in DRF on the affected side. In addition, did the CTT differ on the first renogram in patients who had a pyeloplasty and those who did not undergo surgery. Schlotmann et al[6], Piepsz et al[7] and Harper et al[8] used the time of arrival of activity in the subcortical structures as a measure of the CTT.

Method

The Department of Nuclear Medicine at Red Cross War Memorial Children's Hospital has a database in which all radiopharmaceutical doses, investigations done and reports are recorded and an electronic archive containing the raw data of all studies done since December 2000.

A database search was performed for patients who had at least two renograms between December 2000 and 31st August 2015. The hospital folders of these patients were then reviewed to confirm the diagnosis of unilateral HN with a normal contralateral kidney. A normal contralateral kidney was defined as a kidney with an APD < 10mm and normal corticomedullary differentiation on US. One hundred and seventy eight (178) patients were identified and 110 excluded; 105 did not have an US report in the clinical notes and 5 had an APD of less than 10mm, leaving 68 patients.

All renograms were performed using ^{99m}Tc MAG3 (Mallinckrodt Medical), with the dose determined using the EANM dose card[9, 10]. Patients were hydrated IV prior to injection

of ^{99m}Tc MAG3 with 100 to 200mls of 0.9% NaCl solution. The F+20 protocol was used as recommended in the Guidelines for standard and diuretic renogram in children[4,11], with 1.0mg/kg furosemide being administrated up to a maximum of 20mg.

The raw data was acquired with a Philips Axis Dual Head camera (Picker International Inc., Cleveland, Ohio, USA) with a low energy high resolution (LEHR) collimator on a 128 x 128 matrix. The duration of the renogram was 42 minutes: 1s/frame for the first 2 minutes, 15 second/frame for 40 minutes. The child was then held erect or stood up for 5 minutes after which a static post micturition post gravity drainage image was acquired for 5 minutes.

The raw data was retrieved from the electronic archive and reprocessed. The visual procedure described by Piepsz et al[7] was used to determine CTT. The time of arrival of activity in the subcortical structures, calyces of the upper, middle and lower third of each kidney and pelvis were recorded. The mean of the times activity appeared in the calyces was used as the CTT of the kidney. Each renogram was processed three times on the HERMES Gold ™ software package to measure the DRF using the RP and Integral methods[4, 11]. The mean of the three DRF measurements was used for analysis.

The study was approved from the Human Research Ethics Committee of the University of Cape Town (HREC Reference no 839/2015, see approval in appendix IV).

Statistical analysis

Statistical analysis was performed using the Stata software package (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP). The Shapiro Wilks test was used to test distribution. The median, 25th and 75th centiles, and

minimum and maximum were used as descriptive statistics. The Wilcoxon signed rank test was used for paired data and the Mann Whitney U test to compare groups. Spearman rank correlation test used to assess the association between variables.

Results

Patient demographics

Of the 68 patients with unilateral HN and a normal contralateral kidney, 43 were male and 25 were female. The median age at presentation for the initial renogram was 2.2 months (range 0.2 – 115.3months). Thirty six (36) had left sided HN, with a median CTT of 6 minutes and 32 right sided HN with a median CTT of 6.7 minutes on the initial renogram. The median APD of the left and right HN kidneys were 18.3mm and 23mm respectively (Tables 1 and 2).

Comparing DRF and CTT in the patients who did not have a pyeloplasty

Table 3 summarises the DRF and CTT in the normal contralateral kidneys and the left and right HN kidneys of the 48 patients who did not have a pyeloplasty. There was no difference between DRF of the first and second renograms ($z = -0.858$, $p > 0.05$, $n=47$; in the first renogram of one child, the left hydronephrotic kidney extended to the body outline, making it impossible to draw the standard regions of interest used to calculate DRF). In five patients, there was a drop of more than 10% in the DRF but no record of the reasons for not doing a pyeloplasty. The ages of these patients ranged between 0.1 – 43.2 months, and the APDs ranged between 11.4 and 40mm. In the first renogram, the longest CTT in a normal kidney was 3 minutes, while the shortest CTT in a hydronephrotic kidney was 3.7 minutes. In 32 of the 48 patients, the second renogram showed a decrease in CTT with the CTT of one hydronephrotic kidney falling into the

range of the CTT of normal kidneys. The change in the CTT of the first and second renograms was significant ($z = 4.029$, $p < 0.0001$). Figure 1 illustrates the relationship between the CTT and DRF in the first renogram of the patients who did not have a pyeloplasty ($\rho = -0.2731$, $p < 0.05$) and Figure 2 the relationship between CTT and APD ($\rho = 0.2864$, $p < 0.05$)

Comparing DRF and CTT in the patients who had a pyeloplasty

In the 20 patients who had a pyeloplasty, there was a drop of more than 10% in the DRF of three patients. No difference was seen in the DRF ($z = 0.355$, $p > 0.05$) or in the CTT ($z = 1.217$, $p > 0.05$) between the first and second renogram. CTT was shorter in the second renogram in nine of the 20 patients who had a pyeloplasty.

No significant difference was found in the CTT ($z = -0.054$, $p > 0.05$) or DRF ($z = 0.452$, $p > 0.05$) when comparing the group who had surgery against the group who did not have surgery.

Data of pyeloplasty group compared to the control group

The indication for doing or not doing a pyeloplasty was not clearly stated in the clinical notes of every patient so we undertook a supplementary analysis in those patients who had a pyeloplasty. Each of the children who had a pyeloplasty was matched with a child who did not have surgery based on age within a month and APD within two standard deviations from the median of the APD of the patients who had surgery. The control group was selected from the 48 patient who did not undergo pyeloplasty. Fifteen (15) of the patients were male and five (5) were female with a median age of 1.9 months (range 0.2 – 86.4 months). Twelve (12) had left sided HN, with a median CTT of 6.3 minutes and eight(8) right sided HN with a median CTT of 6.5 minutes. The median APD of the

left and right HN kidneys were 21.6mm and 25mm respectively. The results of the control group are presented in Table 4.

The median interval between the initial renogram and pyeloplasty was 2.7 months (range 0.2 – 72 months) and the median interval between the first and second renogram was 5.2 months (range 0.46 – 22.2months). The pyeloplasty was performed between the first and second renogram. In the control group, the median interval between the first and second renogram was 4.4 months (range 0.1 – 31.8 months).

Table 5 presents the CTT and DRF of the pyeloplasty group and the control group. There was no difference in CTT ($z = -0.027$, $p>0.05$) or DRF ($z = -1.799$, $p>0.05$) on the first renogram but a deterioration in DRF of more than 10 % was seen in three patients on their post pyeloplasty renogram. Figure 3 illustrates the relationship between the CTT ($\rho= 0.3418$, $p >0.05$) and DRF ($\rho= 0.0950$, $p >0.05$).

Discussion

The mean CTT of the left and right hydronephrotic kidneys were 6.0 minutes and 6.7 minutes respectively. An inverse relationship was demonstrated between CTT and DRF in the first renogram of patients who did not have a pyeloplasty. In these patients, patients with prolonged CTT had a larger APD.

There was no difference between the DRF of the first and second renograms in those patients who did not have a pyeloplasty. In the 20 patients who had a pyeloplasty, there was a drop of more than 10% in the DRF of three patients. No difference was seen in the DRF or in the CTT between the first and second renogram. The CTT was shorter in the second renogram in nine of the 20 patients who had a pyeloplasty. No significant

difference was found in the CTT or DRF when comparing the group who had surgery against the group who did not have surgery.

Most children with an antenatal diagnosis of HN do not require surgical intervention[1, 2]. Those likely to benefit from a pyeloplasty are usually symptomatic[11] or identified using an imaging modality. Currently the most widely used practice is serial imaging with US and diuretic renography to detect the earliest signs of a progression in the HN or deterioration in the DRF[12].

Several reports have described the use of CTT to predict deterioration in the function of the hydronephrotic kidney[6-8, 13, 14, 15]. The use of this parameter stems from the postulate that in an obstructed kidney, there is an increase in the pelvic pressure which will lead to a decrease in the renal blood flow, thereby a decrease in the glomerular filtration rate[16]. This ultimately leads to activation of the renin angiotensin system with a series of events which leads to sclerosis. Sclerosis is a very late event in renal outflow obstruction. Increased intrarenal pressure from PUJ obstruction is enough to impair GFR and lead to prolongation of CTT. Therefore, the effect is decreased washout of radiotracer from the renal parenchyma on scintigraphy[6, 16].

The studies performed by Schlotmann et al[6], Piepsz et al[7] and Harper et al[8] all demonstrated the feasibility of using the time of arrival of activity in the subcortical structures as an index for CTT to predict the kidneys which would benefit from surgical intervention. Neither Schlotmann nor Harper report the time of appearance of activity in the subcortical structures in normal or hydronephrotic kidneys. They only state that the time of appearance of activity in the hydronephrotic kidneys was abnormal. The CTTs in the HN kidneys in our study were comparable to those in Piepsz's study (3 – 8

minutes) [7]. In our patients, the CTT of each hydronephrotic kidney was longer than the CTT of the normal contralateral kidney on the first renogram.

In our patients, there was a significant change in CTT between the first and second renogram in those patients who did not have a pyeloplasty. Thirty two (32) of the 48 patients showed a drop in the CTT between the first and second renogram. This is in contrast with Harper and Schlotmann's groups, where Harper et al[8] only identified two patients with abnormal CTT who did not have surgery. One patient had an improvement in their CTT, and the other had a deterioration in their CTT. It is not stated whether this patient had further intervention. Schlotmann et al[6] identified three of 14 patients with abnormal CTT who had no surgery of which two deteriorated and one remained stable. The change in the CTT was not reported in Piepsz' group[7] between the first and second renogram.

There was no significant change in DRF between the first and second renogram in our patients who did not have a pyeloplasty. A drop of more than 10% in the DRF between the first and second renogram was seen in five, a frequency consistent with Josephson[1]. Despite the fact that a drop in DRF of more than 10% in subsequent studies is an acceptable criterion for a pyeloplasty, the CTT did not identify these patients who may have qualified for surgery. In the ten patients who had no surgery in Piepsz's group[7], four had a deterioration in their DRF, with the remaining six patients having no deterioration in DRF.

We were also able to assess if there was a significant difference in the CTT and DRF in the group of patients who had a pyeloplasty and compare them to the patients who did not have surgery as well as a control group. This was not demonstrated in our study. Three patients were identified who had a deterioration in DRF of more than 10 % on

their post pyeloplasty renogram. We were unable to identify reasons for this deterioration from the clinical records. In comparison, Harper et al[8] showed an improvement in CTT post pyeloplasty (however this was not quantified); Schlotmann et al[6] demonstrated in eight out of 13 an improvement in the CTT post-surgery. Piepsz et al[7] demonstrated in ten of the 16 patients who had surgery had an improvement in the DRF. The remainder of the patients showed no significant change in DRF.

Limitations of the study

One of the limitations of this study was that it was retrospective, relying on the standard hospital record system to access data relating to the US information and notes on surgery. There was missing data in terms of the US reports and the indications for the pyeloplasty and reasons for not doing a pyeloplasty were not clearly recorded in some of the notes.

Conclusion

The current study was unable to demonstrate in our series of patients that CTT can predict those patients who would require pyeloplasty. As stated previously, this may be owing to our study being retrospective and our reliance on the clinical notes for the US data and surgical notes.

In future, a prospective study evaluating the relationship between CTT and a drop in the DRF should be undertaken in this unit.

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TABLES

Table 1 Summary of data of all patients

Sex	Male	43	
	Female	25	
Time between initial and second renogram (months)	Median	4.9	
Age (months)	Median	2.2	
	Range	0.24 – 115.3	
Affected sides	Left	36	
	Right	32	
Ultrasound data			
	Left side		
APD(mm)	Median	18.3	
	Range	10 – 57	
	Right side		
APD(mm)	Median	23	
	Range	10 – 69.7	
Cortical Transit Time(minutes)			
		Renogram1	**Renogram2**
Left side	Median	6.0	5.3
Right side	Median	6.7	5.7

Table 2 Summary of data of 48 patients who did not have a pyeloplasty

Affected sides	Left	24	
	Right	24	
Ultrasound data			
	Left side		
APD(mm)	Median	17	
	Range	10 – 40	
	Right side		
APD(mm)	Median	21.9	
	Range	10 – 69.7	
Cortical Transit Time(minutes)			
		Renogram1	**Renogram2**
Left side	Median	6.0	5.0
Right side	Median	6.7	5.7

Table 3. CTT and DRF of the normal contralateral left hydronephrotic and right hydronephrotic kidneys of the patients who did not have a pyeloplasty

	Median		**Interquartile range**				**Minimum**		**Maximum**	
			25		75					
	*R1	*R2	R1	R2	R1	R2	R1	R2	R1	R2
Normal contralateral kidney										
Left CTT (minutes)	2		2		2		2		3	
Right CTT (minutes)	2		2		2.5	2.7	2		3	
Left Hydronephrotic										
CTT (minutes)	6	5.0	4.0	3.8	7.0	7.0	3.7	3.0	10	10
DRF (%)	49	47	42	37	53	51	28	3	63	62
Right Hydronephrotic										
CTT (minutes)	6.7	5.7	6.0	4.5	9.5	6.7	4.0	2.0	10	8.3
DRF (%)	42	45	34	33	51	51	1	9	56	56

*R1 – renogram 1

R2 – renogram 2

Please note that the DRF calculations were performed on 47 patients.

Table 4 Summary of data of 20 patients who had a pyeloplasty and the control group

		Pyeloplasty group	**Control group**
Sex	Male	12	14
	Female	8	6
Age (months)	Median	1.6	2.2
	Range	0.2-86.4	0.7-77.9
Affected sides	Left	12	13
	Right	8	7
Ultrasound data			
	All		
APD(mm)	Median	24	21.4
	Range	12 - 57	10-46
	Right side		
APD(mm)	Median	25	19
	Range	14 - 50	11.5-46
	Left side		
APD(mm)	Median	21.6	24
	Range	12 - 57	10-39
Cortical Transit Time			
Left side	Median	5.8	6.0
Right side	Median	6.5	7.3

Table 5 Quantitative Data relating to the patients who had surgery against the patients who are part of the control group comparing CTT and DRF

	Median		**Interquartile range**				**Minimum**		**Maximum**	
			25		75					
	*R1	*R2	R1	R2	R1	R2	R1	R2	R1	R2
Pyeloplasty patients										
CTT (minutes)	6.3	5.5	5.0	4.7	7.8	7.0	4.0	4.0	10.0	10.0
DRF (%)	46	44	41	32	50	49	18	16	56	57
Control group										
CTT (minutes)	6.3	4.7	5.5	3.8	7.5	6.3	4.0	3.0	10.0	8.3
DRF (%)	50	49	46	42	53	52	29	12	63	58

*R1 – renogram 1

R2 – renogram 2

FIGURES

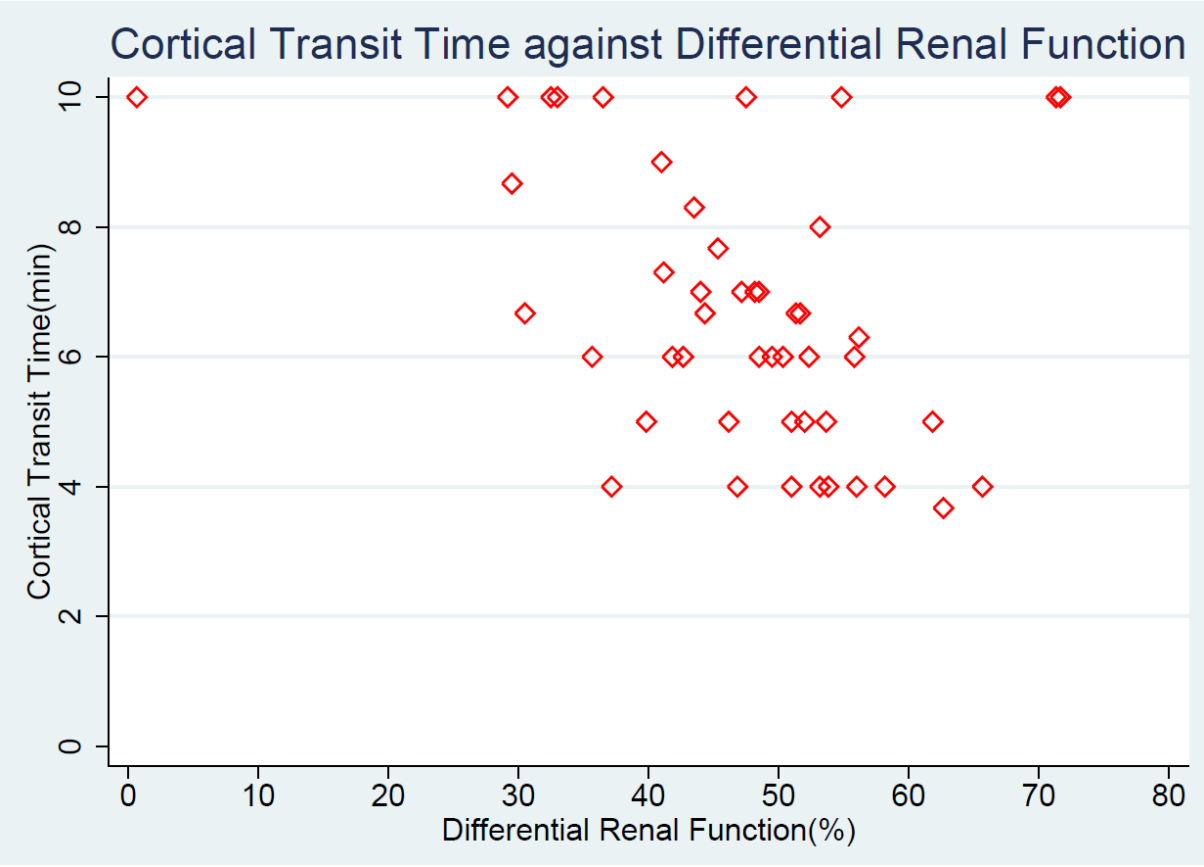

Fig1: CTT vs DRF in those kidneys which did not have a pyeloplasty

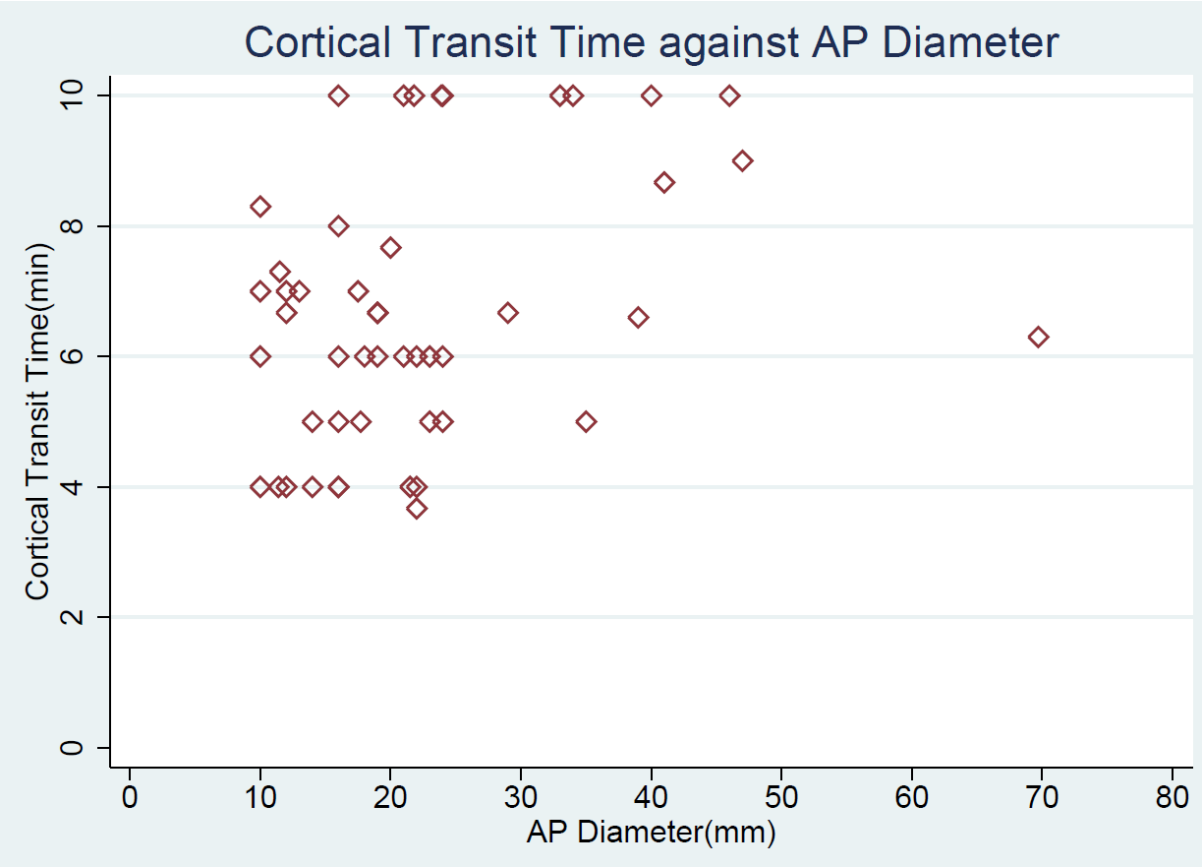

Fig2: CTT vs APD in kidneys which did not have a pyeloplasty

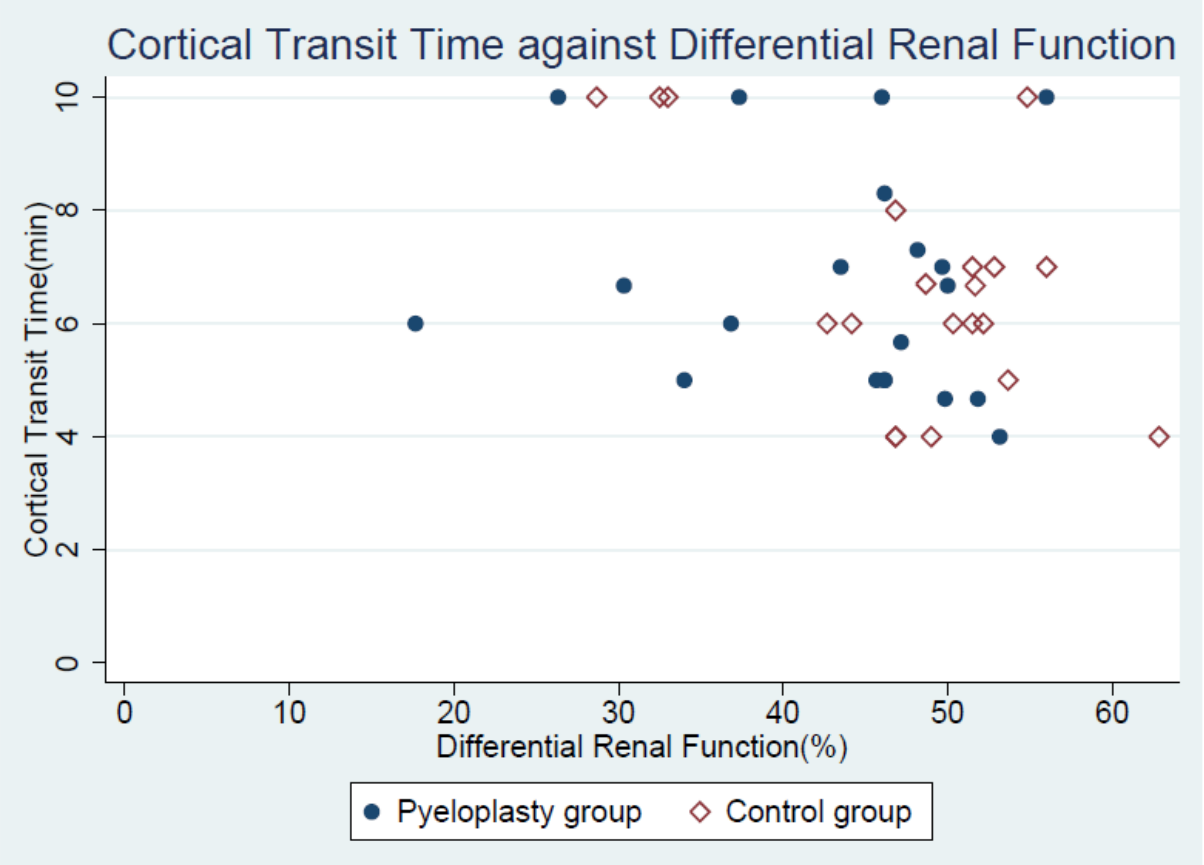

Figure 3: CTT vs DRF: Pyeloplasty group vs control group

APPENDIX I: RESEARCH PROTOCOL

This research protocol was submitted to the Faculty of Health Sciences, University of Cape Town before commencement of the study.

Title of Study:

Renal cortical transit time as a predictor for pyeloplasty in paediatric patients with unilateral hydronephrosis.

Background:

Hydronephrosis (HN) is defined as dilatation of the renal collecting system regardless of the aetiology. The majority of cases which are detected antenatally are asymptomatic and generally will not require any surgical intervention. This was shown in a critical review by Josephson, who found that 88% of those cases who had unilateral HN detected antenatally did not require any urological surgical intervention[1]. The causes of HN that may require intervention are varied, with pelvi-ureteric junction (PUJ) obstruction being the most common, closely followed by vesicoureteral reflux (VUR), obstructive mega ureter and ureterocoele[2].

Literature Review:

According to a definition by Koff, obstruction to a kidney is defined as "any impairment of renal outflow that, left untreated, would lead to a loss of renal function or would prevent the normal maturation of renal function".

This definition of obstruction is retrospective as it is based on a deterioration of the differential renal function (DRF) [3].

In those patients who would require urological surgical intervention owing to PUJ obstruction, a pyeloplasty is the procedure of choice.

A pyeloplasty is a surgical procedure which provides dependent drainage of urine from the hydronephrotic kidney. Factors which are strongly considered for pyeloplasty are

in those patients with symptomatic obstruction (that being recurrent flank pain), a decrease of split function of more than 10% in subsequent studies and complications such as urinary tract infections. Other parameters such as impaired split function (<40%), grade III/IV renal pelvic dilatation with associated parenchymal thinning (as defined by the Society for Fetal Urology) and poor drainage of tracer after the administration of furosemide are considered to a lesser extent in determining which patients will benefit from a pyeloplasty[4].

The prolonged tissue tracer transit time (also called the cortical transit time(CTT)) of ^{99m}Tc MAG3 was reviewed by Schlotmann in an initial study in which he demonstrated on animal models that a delay in CTT accompanied a decline in renal function and associated histomorphological changes in those animal models with unilateral HN[5].

This concept was then applied by Schlotmann to a series of patients who had unilateral HN with a normal contralateral kidney detected on US. One hundred and fifteen (115) patients were part of the sample analysed. Twelve percent of the 115 patients (which equated to 14 patients) in Schlotmann's study were identified as having delayed cortical transit time. Of the 14 patients in this study, 10 of them required surgery in order to prevent further decline. Eight (8) of these patients then improved post-surgical intervention. This demonstrated that kidneys with delayed cortical transit do have the ability to improve after therapy. The CTT can be used as a predictor for those patients who will require surgical intervention in order to preserve the function of a unilateral hydronephrotic kidney (in those patients who had a normal contralateral kidney) [6].

Piepsz and colleagues aimed to verify Schlotmann's statement of CTT having a predictive role in predicting functional impairment. They found that the cortical transit was a valuable tool in identifying those patients who could benefit from a pyeloplasty, with 10 out of 16 patients showing a significant improvement in the DRF post pyeloplasty[7].

Another group, Harper and colleagues, reviewed both Schlotmann's and Piepsz's work to ascertain whether an initial measurement of the CTT correlated significantly with the need for surgery. Thirty seven (37) patients were identified with unilateral HN with a pelvic diameter of 12mm and Piepsz's model was applied to assess CTT. This was defined as absence of activity in the subcortical structures within 3 minutes of tracer injection[7]. Of the 22 patients identified with delayed CTT, 20 of these patients underwent surgery. Harper and colleagues found that the CTT could be used as a reliable prognostic factor in order to map out the future evolution of renal function in those children with HN[8].

A visual assessment tool was used to quantify CTT in all of the above studies. The reason for using a visual assessment tool is twofold. Firstly, methods currently used to quantify CTT, namely deconvolution tools, parametric images which use pixel by pixel time to maximum, mean transit time and factor analysis are not able to differentiate delayed CTT from stasis in the case of an overlapping collecting system. Secondly, the movement of children may impact on the quality of the study and falsely give impression of normal transit especially in the periphery of the kidneys[7, 9].

Objectives:

1) Does the time of arrival of activity in the subcortical structures after tracer injection predict a drop in DRF on the affected side in patients with unilateral HN?

2) Does the visual assessment of CTT in children who went on to have pyeloplasty due to a drop in DRF differ significantly from age and renal pelvis size matched controls?

Methods:

Study Design:

This will be a retrospective study

Patient selection:

The raw data of all renograms performed in the Nuclear Medicine Department at RCWMCH is stored in an electronic database and available for review. All clinical information is stored in a separate database and the names of all patients who had renogram(s) in our department from the 1st of December 2000 will be retrieved.

The inclusion criteria for the first question are:

- Patients with unilateral HN detected on ultrasound with a normal contralateral kidney
- Patients with at least two renograms.

Exclusion criteria:

- Renograms performed for indications other than PUJ syndrome
- Patients with bilateral HN
- Patients with solitary kidneys

- Patients with ectopic kidneys

Patient selection for the second question:

1. All children who went on to have a pyeloplasty will be included; the indication for the pyeloplasty will be recorded.
2. Patients who went on to have a pyeloplasty will be matched to the first patient in the database with matching age and renal AP diameters.

The CTT renal pelvic size matched controls will be based on the anatomical definitions as prescribed by the Society of Foetal Urology[10].

Measurement:

The CTT of the renogram will be assessed visually as described by Piepsz[7].
One minute summed images for the first ten minutes of each study will be evaluated for the appearance of activity in the "calyces".
The DRFs of the study patients will be calculated according to the Patlak-Rutland plot method and integral methods[11].

Ethical considerations:

No patient names will be revealed in any document. The scans performed were part of standard diagnostic tests on each patient which are all in accordance with published international guidelines. All data would be handled in a completely confidential and ethical manner according to the Helsinki Declaration[12].

The study will not affect the running of the Nuclear Medicine, Paediatric Urology or Paediatric Nephrology departments at the hospital.

There are no financial implications for the hospital[12].

References:

1. Josephson S. Antenatally detected, unilateral dilatation of the renal pelvis: a critical review. 1. Postnatal non-operative treatment 20 years on--is it safe? Scand J Urol Nephrol. 2002; 36(4):243-50.

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4. Tekgul S, Dogan HS, Erdem E, Hoebeke P, Kocvara R, Nijman JM, et al. Guidelines on paediatric urology. Arnhem, The Netherlands: European Association of Urology, 2015, pp. 43.

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stenosis detected antenatally might benefit from pyeloplasty? Nucl Med Commun. 2011; 32(3): 199-205

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12. World Medical Association Declaration of Helsinki 2008. Ethical Principles for Medical research Involving Human Subjects. http://www.wma.net/en/30publications/10policies/b3/17c.pdf (Accessed 15 May 2015)

APPENDIX II: DATABASE APPROVAL

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences
Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6626 • **Facsimile** [021] 406 6411
e-mail: shuretta.thomas@uct.ac.za

10 January 2013

REF NO: R009/2012

Dr A Brink
Nuclear Medicine
B5
Red Cross War Memorial Children's Hospital

Dear Dr Brink

PROJECT TITLE: *NUCLEAR MEDICINE DATABASE*

Thank you for registering your database with the Health Sciences Human Research Ethics Committee.

The HREC has approved the registration of your database.

Please Note: All research, including that undertaken for a master's or doctoral degree, using registered databases, registries and repositories, requires submission as a new study. It requires an application form (FHS013) and a protocol which has undergone departmental review. The study will receive its own HREC REF number which will be linked to the main database or repository.

The registration of this database is valid until **30 January 2016.**

Please provide the HREC with an update if the database continues beyond this period.

Please quote the HREC REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

S Thomas

APPENDIX III: ETHICS APPROVAL

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6338 • Facsimile [021] 406 6411
Email: sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

26 November 2015

HREC REF: 839/2015

Dr A Brink
Division of Nuclear Medicine
Room A3.62
Red Cross War Memorial Children's Hospital
Rondebosch

Dear Dr Brink

PROJECT TITLE: RENAL CORTICAL TRANSIT TIME AS A PREDICTOR FOR PYELOPLASTY IN PAEDIATRIC PATIENTS WITH UNILATERAL HYDRONEPHROSIS (MMeD candidate-S More)

Thank you for your response letter, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30th November 2016.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the following student:-Dr Stuart More is also involved in this project.

Please quote the HREC reference no in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research

Hrec/ref:839/2015

APPENDIX IV: DATA SHEETS

Data Sheet

Folder number: _____
Date of Scan: _____
Time of renogram commencement: _____
Time of post micturition image: _____
Date of Birth: _____
Age at Scan: _____
Weight: _____ height: _____

Technical: Include study: Yes/No
If no, state reason: _____

Lasix administered: Yes/No ____ Affected side: _____

			Right kidney			**Left kidney**		
A.	Differential Renal Function (%)	Rutland Patlak						
		Integral						
	NORA							
	ROE (%)	At 20 min						
		At 40 min						
	T half							
B	Date of Ultrasound							
	AP Pelvic diameter (mm)							
	Status of bladder(full/empty)							
	Cortical thinning							
			upper	middle	lower	upper	middle	Lower

C	Time and location of visualisation of activity in the subcortical structures (minutes) Indicate with a tick and description if necessary	1 – 2		
		2 – 3		
		3 – 4		
		4 – 5		
		5 – 6		
		6 – 7		
		7 – 8		
		8 – 9		
		9 – 10		
		>10		
	Visualisation of bladder activity (min)			
	Visualisation of ureter(min)			

D				
	Micturition during the renogram	Yes/no		
	Time of micturition(min)			
	Status of bladder and kidney at the end of the renogram	Kidney(marked /moderate /minimal parenchymal activity)		
		Bladder		
	Post Micturition recorded	Yes/No		
	Kidney counts at	2 min		
	Adequate drainage	Second last summed minute image of renogram		
		Second last image post micturition		

NORA – normalised residual activity

ROE – renal output efficiency

AP – anterior posterior

APPENDIX V: SOUTH AFRICAN JOURNAL OF SURGERY AUTHOR GUIDELINES

Author Guidelines

Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, and will delay publication.

AUTHORSHIP

Named authors must consent to publication. Authorship should be based on substantial contribution to:

(i) conception, design, analysis and interpretation of data;

(ii) drafting or critical revision for important intellectual content; and

(iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to **www.icmje.org**).

CONFLICT OF INTEREST

Authors must declare all sources of support for the research and any association with a product or subject that may constitute conflict of interest.

RESEARCH ETHICS COMMITTEE APPROVAL

Provide evidence of Research Ethics Committee approval of the research where relevant.

PROTECTION OF PATIENT'S RIGHTS TO PRIVACY

Identifying information should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives informed written consent for publication. The patient should be shown the manuscript to be published. Refer to **www.icmje.org**.

ETHNIC CLASSIFICATION References to ethnic classification must indicate the rationale for this.

MANUSCRIPTS Shorter items are more likely to be accepted for publication, owing to space constraints and reader preferences.

Original articles not exceeding 3 000 words, with up to 6 tables or illustrations, are usually observations or research of relevance to surgery. References should preferably be limited to no more than 15. Please provide a structured abstract not exceeding 250

words, with the following recommended headings: *Background, Objectives, Methods, Results,* and *Conclusion.*

Scientific letters/short reports, which include case reports, side effects of drugs and brief or negative research findings should preferably be 1500 words or less, with 1 table or illustration and no more than 6 references. Please provide an accompanying abstract not exceeding 150 words.

Editorials, Opinions, etc. should be about 1000 words and are welcome, but unless invited, will be subjected to the SAJS peer review process.

Review articles are rarely accepted unless invited.

Letters to the editor, for publication, should be about 400 words with only one illustration or table, and must include a correspondence address.

Obituaries should be about 400 words and may be accompanied by a photograph.

MANUSCRIPT PREPARATION Refer to articles in recent issues for the presentation of headings and subheadings. If in doubt, refer to 'uniform requirements'
- **www.icmje.org**. Manuscripts must be provided in **UK English**.

Qualification, affiliation and contact details of ALL authors must be provided in the manuscript and in the online submission process.

Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dl). Litres is denoted with a lowercase 'l' e.g. 'ml' for millilitres). Units should be preceded by a space (except for %), e.g. '40 kg' and '20 cm' but '50%'. Greater/smaller than signs (> and 40 years of age'. The same applies to ± and º, i.e. '35±6' and '19ºC'.

Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160...

Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
Round **brackets** (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

General formatting The manuscript must be in Microsoft Word or RTF document format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes, with the exception of Tables).

ILLUSTRATIONS AND TABLES If tables or illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

Tables may be embedded in the manuscript file or provided as **'supplementary files'**. They must be numbered in Arabic numerals (1,2,3...) and referred to consecutively in the text (e.g. 'Table 1'). Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged. Tables must be cell-based (i.e. not constructed with text boxes or tabs), and accompanied by a concise title and column headings. Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'. Figure legends: Fig. 1. 'Title...' All illustrations/figures/graphs must be of **high resolution/quality**: 300 dpi or more is preferable but images must not be resized to increase resolution. Unformatted and uncompressed images must be attached as '**supplementary files**' upon submission (not embedded in the accompanying manuscript). TIFF and PNG formats are preferable; JPEG and PDF formats are accepted, but authors must be wary of image compression. Illustrations and graphs prepared in Microsoft Powerpoint or Excel must be accompanied by the original workbook.

REFERENCES Authors must verify references from the original sources. *Only complete, correctly formatted reference lists will be accepted.* Reference lists must be generated manually and **not** with the use of reference manager software. Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6] All references should be listed at the end of the article in numerical order of appearance in the **Vancouver style** (not alphabetical order). Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus. Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al. First and last page, volume and issue numbers should be given. **Wherever possible, references must be accompanied by a digital object identifier (DOI) link and PubMed ID (PMID)/PubMed Central ID (PMCID).** Authors are encouraged to use the DOI lookup service offered by **CrossRef**.

Journal references: Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. [http://dx.doi.org/10.1000/hgjr.182] [PMID: 2764753]

Book references: Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101. *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA jun, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.

Internet references: World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: World Health Organization, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).

Other references (e.g. reports) should follow the same format: Author(s). Title. Publisher place: publisher name, year; pages. Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'. Unpublished observations and personal communications in the text must not appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

PROOFS A PDF proof of an article may be sent to the corresponding author before publication to resolve remaining queries. At that stage, **only** typographical changes are permitted; the corresponding author is required, having conferred with his/her co-authors, to reply within 2 working days in order for the article to be published in the issue for which it has been scheduled.

CHANGES OF ADDRESS Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

CPD POINTS Authors can earn up to 15 CPD CEUs for published articles. Certificates may be requested after publication of the article.

CHARGES There is no charge for the publication of manuscripts.

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. Named authors consent to publication and meet the requirements of authorship as set out by the journal.
2. The submission has not been previously published, nor is it before another journal for consideration.
3. The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.
4. The manuscript is in Microsoft Word or RTF document format. The text is single-spaced, in 12-point Times New Roman font, and contains no unnecessary formatting.
5. Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (preferably TIFF or PNG). These must be submitted as 'supplementary files' (not in the manuscript).
6. For illustrations/figures or tables that have been published elsewhere, the author has obtained written consent to republication from the copyright holder.

7. Where possible, references are accompanied by a digital object identifier (DOI) and PubMed ID (PMID)/PubMed Central ID (PMCID).
8. An abstract has been included where applicable.
9. The research was approved by a Research Ethics Committee (if applicable)
10. Any conflict of interest (or competing interests) is indicated by the author(s).